IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 4114
Jin LIU and Ronald FARIS	Examiner: AFREMOVA, Vera
Application No.: 10/574,163	Technology Center/Art Unit: 1657
Filed: March 29, 2006	**DECLARATION UNDER**
For: IMMORTALIZED HEPATOCYTES	**37 C.F.R. § 1.131**
Customer No.: 20350	

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. We, Jin Liu (Sr Research Scientist) and Ronald Faris (President and Chief Scientific Officer), were at the time of the invention employed by Multicell Technologies. While at MultiCell, Dr Liu led the cell immortalization program under the scientific direction of Dr. Faris. We are the named and true inventors of the subject matter disclosed and claimed in the above-referenced patent application.

2. The present invention provides a virally-immortalized hepatocyte having the characteristics of (a) being derived from a normal liver cell; (b) being nontumorigenic; (c) naturally producing endogenous therapeutic plasma proteins (TPPs); and (d) being stable in culture and not undergoing dedifferentiation in culture. The invention is exemplified by hepatocyte cell lines Fa2N-4 and EalC-35.

3. We conceived of and reduced to practice the claimed invention in the United States prior to October 27, 2002, the publication date of Mills, *et al.*, *Drug Metab Rev* (2002) 34:124,

Abstract #248 (Mills). The attached Exhibits A-E are pages from notebooks of scientists at Multicell Technologies who were working under our supervision. The data in the notebook pages provide evidence of the conception of the invention and its reduction to practice before October 27, 2002. The data accompanying this Declaration, with dates redacted from all documents, are as follows:

a. Exhibit A, page 69 describes the donor cells used for creating the Fa2N-4 cell line
b. Exhibit B, page 116 describes the date of transfection of cryopreserved donor hepatocytes to create the original cell clones
c. Exhibit C, page 11 describes selecting the original clones
d. Exhibit D, page 14 describes the subcloning of the Fa2n-4 cells to create the cell line
e. Exhibit E provides an inventory list of numerous different heptocyte cell lines produced at Multicell, created and frozen prior to October 27, 2002

4. Exhibits A-D demonstrate conception and reduction to practice of the exemplified cell line Fa2N-4.

5. Exhibit E demonstrates conception and reduction to practice of the claimed genus of virally-immortalized hepatocytes having the characteristics of (a) being derived from a normal liver cell; (b) being nontumorigenic; (c) naturally producing endogenous therapeutic plasma proteins (TPPs); and (d) being stable in culture and not undergoing dedifferentiation in culture, including the exemplified hepatocyte cell lines Fa2N-4 and EalC-35.

6. In view of the foregoing, we respectfully submit that the evidence provided in Exhibits A through E unequivocally establishes that the claimed invention was conceived of and reduced to practice prior to October 27, 2002.

7. We further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

8. The Declarants have nothing further to say.

Dated: 10/23/08

Jin Liu

Dated: October 22, 2008

Ronald Faris

Attachments
JLW:jlw
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